

11.

Carcinoma of the Pancreas of Acinar Origin in a Bear.¹

PHILIP J. KRESKY, M. D.

&

ROY N. BARNETT, M. D.

(Plates I & II).

CARCINOMA OF THE PANCREAS.

Malignant tumors of the pancreas in animals are of sufficient rarity to warrant the report of an individual case. A review of the literature reveals only eleven well-authenticated cases of carcinoma of the pancreas in mammals; of these, five were in domestic animals, one in a horse (1), three in dogs (2), (3), and one in a cat (4). The six cases in captive wild animals included two in mice, (3), two in monkeys, one in a jackal and one in an Indian civet (5). Balozet & Chainet (1) reporting an adenomacarcinoma of the pancreas in a horse, state that malignant tumors of the pancreas are extremely rare in all the mammalian orders with the exception of carnivora and primates. This statement is confirmed by Slye, Holmes & Wells (6), who performed autopsies on 125,000 mice dying of natural causes. They found 20,000 tumors, of which only two were carcinomas of the pancreas. Ratcliffe (5), in reviewing autopsies on 3,400 mammals and 6,898 birds from the Philadelphia Zoo, found 96 tumors in mammals, 65 of which were malignant and 28 benign. Six were pancreatic tumors, two benign adenomas and four carcinomas. Of 82 tumors found in 6,898 birds, only one was a pancreatic tumor. This was an adenocarcinoma of the pancreas in a fantail grackle. The only malignant pancreatic tumor in the reptilian class (4) was reported by Ratcliffe (7) in a Say's pine snake; on histologic examination this proved to be an adenocarcinoma. Only two of the tumors mentioned (2), (5), had organ metastases. One of these was the case reported by Bru, in a dog with carcinoma of the pancreas, composed of epithelioid cords of large clear cells. He believed that the tumor had its origin in the Islands of Langerhans. Metastatic foci were found in the lung, heart and liver. The other case was that of a jackal discussed by Ratcliffe. This was a medullary carcinoma with liver metastases. With the exception of Bru's case and the case of Nocard referred to by Kitt (3), which lacked a histologic description, all of the malignant tumors were thought to have their derivation from either the ductal or acinar portions of the pancreas. Five were adenocarcinomas (5), (6), two were scirrhous carcinomas (3), (4), one was a medullary carcinoma (5) and one was an adenocarcinoma with areas containing primitive cells of an embryonal type (1).

In no instance was the diagnosis made before death. No clinical syndrome, comparable to that seen in humans, can be constructed from the

¹ From the New York Zoological Park and the Laboratories of The Mount Sinai Hospital.

available data. The only case in which jaundice was seen during life, was reported by Scott & Moore (4). This was a cat with a scirrhus carcinoma involving the head and body of the pancreas and constricting the common bile duct.

Our case is the first in which a carcinoma of the pancreas was found in a bear. Ratcliffe's (6) series included sixty bears on which autopsies were performed. He found four instances of carcinoma; these included a medullary carcinoma of the mammary gland, a basal cell carcinoma of the tongue, an adenocarcinoma of the adrenals, and hypernephroma of the kidney. The only other reported instance of a malignant tumor in a bear was reported by Perry (8). This was a 34-year-old animal with an adenocarcinoma of the kidney.

CASE REPORT.

The large Kadiak bear, whose case is reported here, was captured as a cub in 1907 on Kadiak Island, Alaska, and presented to the New York Zoological Park. He grew and developed normally, reaching a weight of approximately 450 kilograms. He was well until February, 1938, when loss of appetite and weight were noticed. His course was steadily downhill until in August, 1938, he was too weak to stand. At no time was icterus or any other localizing sign or symptom noted. His weight had dropped to approximately 160 kilograms when he was destroyed on August 4, 1938, at the estimated age of 31 years.

POST MORTEM EXAMINATION.

The Mount Sinai Hospital Autopsy No. Z-300; New York Zoological Park No. m-155-38.

Gross: The specimen was an emaciated, adult, male Kadiak bear, *Ursus middendorffi* Merriam, about eight feet total length and weighing approximately 160 kilograms. His fur was lustreless, sparse, brittle and pulled out easily. Over the upper inner aspect of each buttock was a small shallow decubitus ulcer. A firm pedunculated tumor, about the size of a plum, hung from the outer aspect of the upper one-third of his right thigh. This had a narrow stalk and was covered by skin.

The superficial fat was almost lacking. The heart and lungs were not unusual, except for the pale, gelatinous appearance of the epicardial fat. There was no ascites. In the head of the pancreas, behind the descending portion of the duodenum, was a large, elliptical, stony hard tumor, measuring 8 by 6 by 3 cm. (Pl. I, Fig. 1). The common bile duct passed over the anterior aspect of the tumor, but was neither narrowed nor infiltrated. On cut section, the tumor was salmon-colored and the surface was traversed by interlacing bands of glistening white fibrous tissue. Many soft cystic areas, containing semi-liquified tissue, were found in the tumor. The body of the pancreas appeared normally lobulated. The pancreatic duct could not be found. The retroperitoneal lymph nodes, posterior to the tumor, were as large as hazel nuts, firm, and on section contained gray-white areas. The liver was huge, weighing 5,560 grams (Pl. I, Fig. 2). The surface was studded with large round pink-white metastatic nodules, some umbilicated and ranging from one to eleven cm. in diameter. On section, much of the liver parenchyma was replaced by pink-white circumscribed round foci similar to those seen on the surface. Many of these metastatic nodules contained areas of necrosis and hemorrhage. No other tumor metastases were found. An incidental finding was the presence of numerous, large, faceted stones in the gall bladder, whose wall was somewhat thickened. The large biliary radicles were all patent. No unusual changes were noted in the remaining viscera.

Microscopic: The tumor in the pancreas, liver and lymph nodes had essentially the same histologic appearance. There were two types of cell patterns. In one the cells were arranged in definite pseudo-acinar groupings (Pl. II, Figs. 3A and 4A) or in thick, tortuous cords having papillary projections. The cells had large vesicular hyperchromatic nuclei with prominent deep-staining nucleoli. Mitotic figures were infrequent. The cytoplasm was abundant and contained innumerable eosinophilic zymogen granules (Pl. II, Fig. 3B). The zymogen granules in the pseudo-acinar structures were situated on the side of the cells next to the lumen, and pushed the nuclei to the base of the cell. The other predominating cell pattern consisted of epithelioid cords of small cells, many with dark pyknotic nuclei. (Pl. II, Fig. 4B). The cytoplasm was scant and filled with vacuoles which took the Sudan III stain for neutral fat. Some of the cells in these cords contained zymogen granules. The stroma of the tumor consisted of a loose, delicate, highly vascular connective tissue framework. No portion of the carcinoma resembled the Islands of Langerhans. Sections of the pancreas immediately adjacent to the primary tumor showed atrophy of the parenchyma and dense interstitial fibrosis. Histologic study of the rest of the pancreas revealed slight lipomatosis.

COMMENT.

Ordinarily pancreatic tumors arise from either the ducts or the Islands of Langerhans. Histologic examination proved our tumor to be a parenchymal cell carcinoma, having its origin in the acinar tissue of the pancreas. The most unusual feature was the presence of zymogen granules in the cells. This is a definite indication that active secretion and elaboration of pancreatic enzymes was occurring, and on this basis the origin of the tumor in pancreatic acinar cells can be postulated. In some of the other glandular organs, carcinomas producing secretion are well-known. Hepatomas of the liver produce bile and have the same metabolic functions as normal liver cells. Symptoms of Grave's disease may be associated with adenocarcinomas of the thyroid gland. However, in only one pancreatic carcinoma in the literature was acinar origin proved by the presence of secretion. This was the case of Sugiura, Pack & Stewart (9) who proved the presence of active enzymes in a human pancreatic adenocarcinoma. Their tumor was considered histologically characteristic of an acinar adenocarcinoma, but no mention of the presence of zymogen granules was made. They found that the tumor contained as much protease and lipase and more amylase than normal human pancreas.

SUMMARY.

A case of primary parenchymal cell carcinoma of the pancreas with extensive liver metastases is reported. The significance of zymogen granules pointing to acinar cell origin is discussed.

BIBLIOGRAPHY.

1. BALOZET, L. & CHAINET, L.: Primary Epithelioma of the Pancreas in a Horse. *Bull. Acad. Vet.* 10:301, 1937.
2. BRU, P.: Cancer Langerhansien Généralise chez un Chien. *Rev. Medico-Chirurgicale des Maladies du Foie, du Pancreas, et de la Rate.* 2:40, 1927.
3. KITT, T.: *Lehrb. d. path. Anat. d. Haustiere*, 1921, 600.
4. SCOTT, E. & MOORE, R. A.: A case of Pancreatic Carcinoma in a Cat. *J. of Cancer Research.* 11:152, 1927.
5. RATCLIFFE, H.: Incidence and Nature of Tumors in Captive Wild Mammals and Birds. *A. J. Cancer.* 17:116, 1933.

6. SLYE, M., HOLMES, H. F. & WELLS, H. G.: Comparative Pathology of Carcinoma of the Pancreas. *A. J. Cancer.* 23:81, 1935.
7. RATCLIFFE, H.: Carcinoma of the Pancreas in Say's Pine Snake. *A. J. Cancer.* 24:78, 1935.
8. PERRY, C. B.: Carcinoma of the Kidney in a Bear. *J. Comp. Path. and Therap.* 42:133, 1929.
9. SUGIURA, PACK & STEWART: A Study of the Enzyme Content of a Parenchymatous Adenocarcinoma of the Pancreas and a Comparison with the Normal Human Pancreas. *A. J. Cancer.* 26:351, 1936.

EXPLANATION OF THE PLATES.

PLATE I.

- Fig. 1. Primary carcinoma of pancreas. **D**—Duodenum. **S**—Stomach. **T**—Tumor.
 Fig. 2. Liver with metastases.

PLATE II.

- Fig. 3A. Pseudo-acinar structure.
 Fig. 3B. Higher magnification, showing zymogen granules.
 Fig. 4A. More anaplastic area.
 Fig. 4B. Small-cell area, same magnification as 4A.